

## CLAIMS

We claim:

*Pub B12*

1. A protein produced by a method comprising:  
culturing a host cell into which has been introduced a DNA expression vector comprising the following operably linked elements:

a transcription promoter;  
a DNA segment comprising a nucleotide sequence as shown in SEQ ID NO: 1 from nucleotide 76 to nucleotide 417;  
and

a transcription terminator, wherein said host cell expresses the polypeptide encoded by said DNA segment; and recovering said protein.

2. The protein of claim 1, wherein the host cell is a mammalian cell.

3. The protein of claim 1, wherein the host cell has had a second DNA vector introduced into it, wherein said second expression vector comprises the following operably linked elements:

a transcription promoter;  
a DNA segment encoding an endoprotease; and  
a transcription terminator, wherein said host cell expresses the polypeptide encoded by the DNA segment comprising a nucleotide sequence shown in SEQ ID NO: 1 from nucleotide 76 to nucleotide 417; and said DNA segment encoding said endoprotease.

4. An isolated and purified protein comprising:  
a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and  
a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139

(Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating.

5. An isolated and purified protein comprising:  
 a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue selected from the group consisting of 48 (Lys), 49 (Thr) and 50 (Phe); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating.

6. A method of stimulating proliferation of pancreatic islets comprising administering to a mammal in need thereof, an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce a clinically significant increase in insulin secretory capacity in said mammal.

7. The method of claim 6, wherein the clinically significant increase in insulin secretory capacity results in a decrease in fasting plasma glucose levels.

8. The method of claim 6, wherein the isolated and purified protein is administered in combination with an insulin sensitizer.

9. A method of stimulating proliferation of pancreatic islets comprising administering to a mammal in need thereof, an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue selected from the group consisting of 48 (Lys), 49 (Thr) and 50 (Phe); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce a clinically significant increase in insulin secretory capacity in said mammal.

10. The method of claim 9, wherein the clinically significant in insulin secretory capacity results in a decrease in fasting plasma glucose levels.

11. The method of claim 9, wherein the isolated and purified protein is administered in combination with an insulin sensitizer.

12. A method for stimulating *in vitro* proliferation of pancreatic islet cells comprising culturing islets with an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce an increase in the number of islet cells as compared to islet cells cultured in the absence of said protein.

13. The method of claim 12, wherein said cells are cultured in 0.1 ng/ml to 100 ng/ml of said protein.

14. A method for stimulating *in vitro* proliferation of pancreatic islet cells comprising culturing pancreatic islets in an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue selected from the group consisting of 48 (Lys), 49 (Thr) and 50 (Phe); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce an increase in the number of islet cells as compared to islet cells cultured in the absence of said protein.

15. The method of claim 14, wherein said cells are cultured in 0.1 ng/ml to 100 ng/ml of said protein.